REMARKS

Reconsideration of the present Application in view of the above amendments and the following remarks is respectfully requested. Claims 3-14 are currently pending. Applicants hereby cancel claims 3-5 and 11 without acquiescence in any rejection and without prejudice to the filing of any related divisional, continuation, or continuation-in-part application. Claims 6, 8, 10, and 12 have been amended to more clearly define the subject matter encompassed by Applicants' invention. Support for the amended claims may be found in the specification, for example, at page 6, line 25 through page 7, line 3; page 9, lines 8-21. No new matter has been added.

REJECTION UNDER 35 U.S.C. § 101 AND 35 U.S.C. § 112, FIRST PARAGRAPH

The PTO rejects claims 3-14 under 35 U.S.C. § 101, alleging that the invention lacks utility. Specifically, the PTO alleges that the claimed polynucleotide lacks a specific, substantial, and credible utility and a well-established utility. The PTO asserts that without a demonstration otherwise, the claimed polynucleotide could have another catalytic activity, such as a phospholipase activity, which the PTO alleges is taught in Acton (U.S. Patent No. 6,268,135). The PTO further asserts that the phosphatase activities of the polypeptides disclosed in U.S. Patent Nos. 6,258,528 and 6,132,964 do not support Applicants' assertion that the presently claimed polynucleotide encodes a dual specificity phosphatase. The PTO alleges that without identifying a specific MAP-kinase that is regulated by DSP-14, or absent identification of any disease with which DSP-14 is associated, a specific and substantial utility is not established.

The PTO also rejects claims 3-14 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. In particular, the PTO asserts that the claimed invention has neither a specific, substantial, and credible utility nor a well-established utility, such that one skilled in the art would not know how to make and use the claimed invention.

Applicants respectfully traverse these grounds for rejection and submit that the Action has not set forth a *prima facie* case showing that the subject matter of the instant claims, *i.e.*, polynucleotides encoding a dual specificity phosphatase-14 (DSP-14) polypeptide,

compositions comprising the DSP-14 encoding polynucleotides, and a method for expressing a DSP-14 polypeptide, lacks utility. Applicants' invention is directed in pertinent part to an isolated polynucleotide that encodes a polypeptide comprising the sequence of DSP-14 set forth in SEQ ID NO:2, wherein the polypeptide has the ability to dephosphorylate an activated MAP-kinase; and to related compositions and methods. In certain embodiments, the invention is directed in pertinent part to an antisense polynucleotide comprising a nucleotide sequence complementary to a polynucleotide that encodes a polypeptide comprising the sequence of DSP-14 set forth in SEQ ID NO:2, wherein the polypeptide has the ability to dephosphorylate an activated MAP-kinase, and wherein the polynucleotide comprises the sequence set forth in SEQ ID NO:1.

Applicants respectfully submit that the presently claimed DSP-14 encoding polynucleotides, and their use in the claimed method for producing a DSP-14 polypeptide, have a well-established and a specific, substantial, and credible utility. Applicants submit that a person having ordinary skill in the art will immediately appreciate the usefulness of the invention based on its characteristics, which are described in the specification and recited in the instant claims. In particular, and as will be presented in a forthcoming Declaration currently in preparation, the claimed polynucleotide encodes a DSP-14 polypeptide that has phosphatase activity. The Declaration will also address the disclosure of Acton (U.S. Patent No. 6,268,135.

Furthermore, and for reasons previously made of record (see Amendment and Response submitted August 6, 2002, in reply to the Office Action dated March 6, 2002), Applicants submit that given the state of the art and the instant disclosure, persons skilled in the art understand that DSP-14 is a dual specificity protein tyrosine phosphatase that dephosphorylates both (i) phosphotyrosine and (ii) phosphothreonine and/or phosphoserine residues (*see, e.g.*, page 2, lines 5-12, and references cited therein; page 6, line 25 through page 7, line 3) on specific substrates such as activated MAP-kinases, the regulation of which is important to the operation and control of conserved cellular signal transduction pathways (*see, e.g.*, page 1, line 22 through page 2, line 4). The presently claimed polynucleotides (*e.g.*, SEQ ID NO:1) encode polypeptides containing a protein tyrosine phosphatase active site motif (*see, e.g.*, specification, page 13, lines 1-2) that is conserved in dual specificity phosphatases (*see, e.g.*,

specification, page 46, lines 8-14, and references cited therein). Furthermore, the full-length DSP-14 polypeptides (*e.g.*, SEQ ID NO:2) encoded by the invention polynucleotides show significant homology to other MAP-kinase phosphatases (*see, e.g.*, specification, page 13, lines 7-8; Figure 3). On the basis of the identified active site motif and the homology of the encoded DSP-14 polypeptide with other dual specificity phosphatase family members, a person having ordinary skill in the art would reasonably believe that the DSP-14 polypeptide described in the instant specification has the *specific* ability to dephosphorylate an activated MAP-kinase. Therefore, such a person having skill in the art would readily understand that a substantial utility of the disclosed invention resides in furthering the understanding of the role of dual specificity phosphatases in MAP-kinase cascades that mediate cellular transduction of biological signals.

Applicants thus respectfully submit that the present invention has a specific, substantial, and credible utility, in full compliance with all requirements of 35 U.S.C. § 101, and request that the rejection be withdrawn.

Moreover, and with regard to enablement, Applicants respectfully traverse the rejection under 35 U.S.C. § 112, first paragraph, and submit that the instant specification provides sufficient disclosure to teach a person having ordinary skill in the art how to make and use the claimed invention. Applicants submit that the present application teaches a skilled person how to make and use, readily and without undue experimentation, an isolated polynucleotide that encodes a DSP-14 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2, wherein the polypeptide has the ability to dephosphorylate an activated MAP-kinase, and related compositions and methods, including a method of producing a DSP-14 polypeptide. As described in the instant specification, the claimed DSP-14 encoding polynucleotide (SEQ ID NO:1) encodes a dual specificity phosphatase-14 polypeptide (SEQ ID NO:2) that has the ability to dephosphorylate an activated MAP-kinase (*see, e.g.*, page 6, line 17 through page 7, line 3). DSP-14 polypeptides may be expressed and isolated, and DSP-14 phosphatase activity assayed, according to methods known in the art and disclosed in the specification (*see, e.g.*, page 9, line 8 through page 10, line 2; page 18, line 2 through page 19, line 24). Applicants submit that all of the aforementioned methods may be performed by permissible routine screening and without undue experimentation.

Accordingly, Applicants respectfully submit that the claimed invention has a specific, substantial, and credible utility, which therefore satisfies the requirements of 35 U.S.C. § 101. Applicants further submit that the specification enables a person having ordinary skill in the art to make and use the claimed invention in full compliance with 35 U.S.C. § 112, first paragraph. Therefore, Applicants respectfully request that the rejection of these claims be withdrawn.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (WRITTEN DESCRIPTION)

The PTO rejects claims 3-5 and 11-13 under 35 U.S.C. § 112, first paragraph, asserting that the claims are directed to subject matter that is not adequately described in the specification. Specifically, the PTO asserts that a specific functional activity is not identified and demonstrated for the claimed polynucleotide. The PTO maintains its allegation that the DSP-14 active site (SEQ ID NO:3) is a generic sequence that is present in other enzymes that are not dual specificity phosphatases, and that would have "no diagnostic value for the asserted utility by the applicants."

Applicants respectfully submit that the grounds for this rejection are obviated in view of the Amendment submitted herewith, which includes cancellation of claims 3-5 and 11 (upon which claims 12 and 13 depended in part), without acquiescence or prejudice. Applicants' invention is directed in certain embodiments to an expression vector comprising an antisense polynucleotide comprising a nucleotide sequence complementary to a polynucleotide that encodes a DSP-14 polypeptide comprising the sequence set forth in SEQ ID NO:2, wherein the polypeptide has the ability to dephosphorylate an activated MAP-kinase, and wherein the polynucleotide comprises the sequence set forth in SEQ ID NO:1, and to a host cell comprising this expression vector. Applicants submit that Applicants possessed the claimed invention, as disclosed in the present specification and recited in the instant claims, at the time the application was filed, thus complying with the requirements of 35 U.S.C. § 112, first paragraph. Applicants therefore respectfully request that this rejection be withdrawn.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (ENABLEMENT)

The PTO rejects claims 3-14 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Specifically, the PTO asserts that the disclosed polypeptide shares very little sequence homology with any dual specificity phosphatase and has the greatest homology to a phospholipase, "which places the asserted utility in doubt." The PTO further alleges that the claimed polynucleotides are not limited with regard to their function, and that absent a three-dimensional structure of the polypeptide having the sequence set forth in SEQ ID NO:2, undue experimentation would be required for a skilled artisan to make and use the invention.

Applicants respectfully traverse this rejection and submit that the specification enables a person skilled in the art to make and use the invention as claimed. Applicants respectfully submit that rejection of claims 3-5 and 11 is rendered moot in view of the Amendments submitted herewith, which includes cancellation of these claims. As noted above, Applicants' invention is directed to isolated polynucleotide that encodes a polypeptide comprising the sequence of DSP-14 set forth in SEQ ID NO:2, wherein the polypeptide has the ability to dephosphorylate an activated MAP-kinase; and to related compositions and methods. In certain embodiments, the invention is directed in pertinent part to an antisense polynucleotide cleotide comprising a nucleotide sequence complementary to a polynucleotide that encodes a polypeptide comprising the sequence of DSP-14 set forth in SEQ ID NO:2, wherein the polypeptide has the ability to dephosphorylate an activated MAP-kinase, and wherein the polynucleotide comprises the sequence set forth in SEQ ID NO:1.

Applicants respectfully submit that the instant specification provides explicit guidance enabling a skilled artisan to make and use the claimed polynucleotides without undue experimentation. Applicants further submit that the aforementioned Declaration currently in preparation will present evidence that the present Application satisfies the requirements of 35 U.S.C. § 112, first paragraph, and for reasons previously made of record, that the claimed polynucleotides encode an enzyme that relates to a phosphatase and not to a phospholipase.

As discussed in the Amendment and Response submitted August 6, 2002, in reply to the Office Action dated March 6, 2002, the specification discloses the polynucleotide sequence (SEQ ID NO:1) that encodes a DSP-14 polypeptide (see SEQ ID NO:2), which is

capable of dephosphorylating a DSP-14 substrate, including activated (*i.e.*, phosphorylated) MAP-kinases (*see, e.g.,* page 6, line 25 through page 7, line 3). The polypeptides expressed can then be analyzed for their ability to dephosphorylate a suitable substrate, such as an activated MAP-kinase, according to assays for detecting DSP-14 activity, which are also described in the specification (*see, e.g.,* page 18, line 1 through page 19, line 24).

To identify whether a polynucleotide as recited in the claims would encode a polypeptide that is capable of exhibiting phosphatase activity, the specification explicitly teaches that the DSP-14 active site comprises the sequence, VHCVMGRSRSATLVLAYLM (SEQ ID NO:3). (*See, e.g.,* specification page 8, lines 24-25; page 13, lines 1-2; SEQ ID NO:2 at amino acid positions 145-163). As understood in the art and disclosed in the present application, dual specificity phosphatases belong to the larger family of protein tyrosine phosphatases that share a conserved catalytic domain containing a cysteine residue situated N-terminal to a stretch of five variable amino acids followed by an arginine residue (*see, e.g.,* specification, at page 46, lines 8-14 and cited reference: Fauman et al., *Trends in Biochem. Sci.* 21:413-17 (1996); see also Jia, *Biochem. Cell Biol.* 75:17-26 (1997); Flint et al., *Proc. Natl. Acad. Sci. USA* 94:1680-85 (1997)). Applicants submit that given the sequence and the location of the amino acids comprising the active site, a person having skill in the art, using alignment methods known in the art and disclosed in the specification (*see, e.g.*, page 10, lines 14-27), can readily identify whether a polynucleotide will encode the active site of a DSP-14 polypeptide.

Accordingly, applicants respectfully submit that the present application satisfies all the requirements of 35 U.S.C. § 112, first paragraph, and therefore request that the rejection of the claims be withdrawn.

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claim 10 stands rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. In particular, the PTO asserts that the claim is directed to 15 contiguous nucleotides of a nucleic acid encoding a protein that is 75% homologous to SEQ ID NO:2, and as such, allegedly encompasses embodiments unknown to a person skilled in the art and incapable of being searched.

Applicants respectfully traverse this rejection and submit that amended claim 10 particularly points out and distinctly claims the subject matter that Applicants regard as their invention. The invention is directed in pertinent part to an antisense polynucleotide comprising a nucleotide sequence complementary to a polynucleotide that encodes a polypeptide comprising the sequence of DSP-14 set forth in SEQ ID NO:2, wherein the polypeptide has the ability to dephosphorylate an activated MAP-kinase, and wherein the polynucleotide comprises the sequence set forth in SEQ ID NO:1. Applicants therefore respectfully submit that claim 10 meets the requirements for definiteness under 35 U.S.C. § 112, second paragraph, and request that this rejection be withdrawn.

REJECTION UNDER 35 U.S.C. § 102

The PTO rejects claims 3-14 under 35 U.S.C. §102(e) as allegedly anticipated by WO 01/46394 (Plowman et al.). More specifically, the PTO asserts that SEQ ID NO:5 disclosed in WO 01/46394 shares 94% identity with SEQ ID NO:1 of the present application, and that the open reading frames of these sequences are 100% identical. The PTO further asserts that the amino acid sequence SEQ ID NO:17 disclosed in WO 01/46394 is identical with SEQ ID NO:2 of the instant application except for the amino acid at position 85, which the Examiner believes results from an error in the listing of either amino acid sequence because the nucleic acid sequences of the open reading frame are identical.

Applicants respectfully traverse this rejection and submit that the subject matter of the present claims is novel. Applicants respectfully submit that rejection of claims 3-5 and 11 is rendered moot in view of the Amendments submitted herewith, which includes cancellation of these claims.

Applicants submit that WO 01/46394 fails to anticipate each and every limitation of the present claims and therefore cannot be novelty-destroying. WO 01/46394 fails to teach or suggest a polynucleotide that encodes a polypeptide comprising the sequence of DSP-14 set forth in SEQ ID NO:2, and further fails to teach or suggest that this polypeptide has the ability to dephosphorylate an activated MAP-kinase. WO 01/46394 also fails to teach or suggest a polynucleotide comprising the sequence set forth in SEQ ID NO:1. The cited reference discloses

a nucleic acid sequence that shares only approximately 94% identity with SEQ ID NO:1. The cited document also fails to teach or suggest an antisense polynucleotide comprising a nucleotide sequence complementary to a polynucleotide that encodes a polypeptide comprising the sequence of DSP-14 set forth in SEQ ID NO:2, wherein the polypeptide has the ability to dephosphorylate an activated MAP-kinase, and wherein the polynucleotide comprises the sequence set forth in SEQ ID NO:1. Therefore, WO 01/46394 fails to teach or suggest an expression vector that comprises the claimed polynucleotides, a host cell comprising such a vector, and a method for producing a DSP-14 polypeptide as recited.

Applicants submit that the claims are novel and comply with the requirements of 35 U.S.C. §102. Applicants therefore respectfully request that this rejection be withdrawn.

All claims remaining in the application are now allowable. Favorable consideration and a Notice of Allowance are earnestly solicited. In the event that the Examiner believes a teleconference will facilitate prosecution of this case, the Examiner is invited to telephone the undersigned at (206) 622-4900.

Respectfully submitted,

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